UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/673,781 | 09/29/2003 | Qinwei Shi | 1112-1-080NDIV | 1672 |

43850 7590 11/20/2006

MORGAN, LEWIS & BOCKIUS LLP (SF)
2 PALO ALTO SQUARE
3000 El Camino Real, Suite 700
PALO ALTO, CA 94306

| EXAMINER | |
|---|---|
| COOK, LISA V | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/673,781 | SHI, QINWEI | |
| | Examiner | Art Unit | |
| | Lisa V. Cook | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24 and 34-47* is/are pending in the application.

4a) Of the above claim(s) *1-24 and 39-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-24 and 34-47* are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of Group III (claims 34-38) in the reply filed on 28 August 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The Restriction Requirement is deemed proper and is therefore made **FINAL.**

2. Claims 1-24 and 39-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/28/06. Currently claims 3-9, 18-28, and 33-35 are under consideration.

### *Priority*

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120 to division application number **09/938,270 filed 8/23/01 now US Patent #6,673,562**, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

4. Please add a reference to divisional application number 09/938,270 filed 8/23/01 now US Patent #6,673,562 to the first line of the disclosure.

***Information Disclosure Statement***

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

6. The information disclosure statement and supplemental information disclosure statement filed 9/29/03 have been considered as to the merits prior to first action.

***Drawings***

7. This application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. The drawings in this application are objected to by the Examiner under 37 CFR 1.821(a)(1) and (a)(2) because the figure contain sequences, which have not been identified appropriately. The sequences must include a sequence identification number. Please submit new formal drawings including the SEQ. ID. NO. Specifically see figure 12A and 12B.

***Sequence Non-Compliance***

8. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. The drawings contain sequences that have not been appropriately identified by sequence identification numbers, see figure 12A and 12B.

Applicant is given THREE MONTS from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

***Specification***

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The use of the trademarks has been noted in this application. (.i.e. TWEEN on page 50. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 35 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 35 the term "capable of" is vague and indefinite because it is not clear if the compounds bind to each other or not? It is suggested that this term be removed from the claim language in order to obviate this rejection.

B. Claim 36 is vague and indefinite because it is not clear if "said antibody" is the first antibody previously bound to a second analyte (claim 35 lines 1-2), the second antibody capable of binding the second analyte (claim 35 last line), or both. As recited the metes and bounds of the claim cannot be determined and one of ordinary skill in the art would not be appraised of the scope of the instant invention. Please clarify the claim.

## *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 34-38 are directed to non-statutory subject matter. The invention as claimed read on any antibody conjugate or polynucleotide encoding said conjugate, where the conjugate compositions or molecules includes products of nature. Non-naturally occurring compositions are considered to be patentable subject matter within the scope of 35 U.S.C. 101. Compositions that are products of nature are considered non-statutory and non-patentable. See Official Gazette, 1077 O.G. 24, April 21, 1987. It is recommended that the claims incorporate the claim language, "isolated" or "purified" to overcome this rejection.

## *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 34-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth a conjugate comprising an antibody bound to carbonic anhydrase III via a single chain polypeptide (SEQ ID NO:1) and its polynucleotide expression product (SEQ ID NO:2) and therefore the written description is not commensurate in scope with the claims drawn to the utility of any fragment thereof.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117).

The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:1 and SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the encompassed binding fragments thereof and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of a compound/seq.id/etc. by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules, usually defined by a sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, no disclosure, beyond full length SEQ ID NO:1 and SEQ ID NO:2 is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only full length SEQ ID NO:1 and SEQ ID NO:2, but not any fragment thereof would meet the full breadth of the claims as required by the written description provision of 35 USC 112, first paragraph.

13. Claims 34-36 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody conjugate wherein the second analyte is carbonic anhydrase III bound to streptavidin and the first analyte is myoglobin, it does not reasonably provide enablement for any and all antibody conjugates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The prior art teaches that antibody engineering must consider various factors (for example, chemical linkage, enzymatic digestion, problems due to each unique amino acid sequence, difficult refolding procedures, and contamination) in order to produce functional protein molecules (antibody conjugates). For example, see Peipp et al. (Biochemical Society Transactions, 2002, Volume 30, part 4, pages 507-511, especially page 510 –Production of bi-specific antibodies). Because the disclosure only sets forth antibody conjugates comprising carbonic anhydrase III bound to streptavidin wherein the first analyte is myoglobin, it does not reasonable teach any and all antibody conjugates as set forth in the claims.

## *Claim Rejections - 35 USC § 102*

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**I.** Claims 34-36 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Koo et al. (Applied and Environmental Microbiology, July 1998, pages 2497-2502).

Koo et al. disclose a streptavidin(second analyte)-conjugated single chain antibody (antibody to first analyte). This bifunctional single chain antibody was developed to measure *B. cereus* T spores. See abstract. The fusion protein was expressed and recovered in DNA plasmids (polynucleotide encoding the conjugate) that were transformed in *E.coli* BL21(DE3). Page 2498 1st column and page 2499 1st column- Results and Discussion. The recombinant fusion antibody functioned essentially in the same manner as the native antibody in immunoassays for pathogen detection while also exhibiting the binding characteristics of streptavidin. Page 2501 2nd column.

## *Claim Rejections - 35 USC § 103*

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**II.** Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Koo et al. (Applied and Environmental Microbiology, July 1998, pages 2497-2502) in view of Vuori et al. (Clinical Chemistry, Vol.37, No.12, pages 2087-2092, 1991).

Please see previous discussions of Koo et al. (Applied and Environmental Microbiology, July 1998, pages 2497-2502) as set forth above.

Koo et al. (Applied and Environmental Microbiology, July 1998, pages 2497-2502) differ from the instant invention in failing to teach carbonic anhydrase III as the second analyte and myoglobin as the first analyte.

However, Vuori et al. discloses that considerable interest exits for methods that quantify two or more antigens or antibodies simultaneously in one sample. This assay system is advantageous in cases where the ratio of the compounds gives relevant information. See page 2087 1st column.

The simultaneous measurement of serum carbonic anhydrase III (S-CA III) and serum myoglobin (S-Mb) can be used to evaluate the origin of muscle-derived proteins as well as differentiate between acute myocardial and skeletal muscle damage. See page 2087 2nd column and page 2090-Discussion.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to construct a bifunctional conjugate as taught by Koo et al. with carbonic anhydrase III and myoglobin as taught by Vuori et al. because Vuori et al. taught that the simultaneous detection of serum carbonic anhydrase III (S-CA III) and serum myoglobin (S-Mb) can be used to evaluate the origin of muscle-derived proteins as well as differentiate between acute myocardial and skeletal muscle damage. See page 2087 2nd column and page 2090-Discussion.

One having ordinary skill in the art would have been motivated to do this because the bifunctional compositions worked as well as their native counterparts. See Koo et al. page 2501 2nd column. Further, allowing for multiple analyte detection in one sample. See Vuori et al. page 2087 1st column.

16. For reasons aforementioned, no claims are allowed.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lisa V. Cook 11/3/06
Lisa V. Cook
Remsen 3C-59
571-272-0816
11/3/06

LONG V. LE 11/05/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600